REMARKS

Claims 4-27, 31-40 and 43-45, which are directed to the non-elected subject matter of Groups II-VI, have been cancelled without prejudice to the filing of a divisional application on the same.

Claims 1-30 were in the application as filed. Claims 31-45 were added in the Preliminary Amendment dated December 19, 2000. Claims 4-27, 31-40 and 43-45 were canceled by the foregoing amendment. Claims 1-3, 28-30 and 41-42 remain in the application.

Claims 1-3, 28 and 41-42 are rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 5,629,331 to Caron et al. In support of this rejection the Examiner has stated that:

> Caron et al. teach crystalline forms of 2-n-butyl-4-spirocyclopentane-1-[(2'-(tetrazol-5-yl)biphenyl-4-yl)methyl]-2-imidazolin-5-one compounds and their use as pharmaceuticals. Applicant discloses a crystalline 2-n-butyl-4-spirocyclopentane-1-[(2'-(tetrazol-5-yl)biphenyl-4-yl)methyl]-2-imidazolin-5-one compound and its use as a pharmaceutical. Caron et al. teach 2-n-butyl-4-spirocyclopentane-1-[(2'-(tetrazol-5-yl)biphenyl-4-yl)methyl]-2-imidazolin-5-one in column 1, lines 40-47. Crystalline forms of 2-n-butyl-4-spirocyclopentane-1-[(2'-(tetrazol-5-yl)biphenyl-4-yl)methyl]-2-imidazolin-5-one and pharmaceutical compositions containing the crystalline form are taught in column 1, lines 10-12.
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> The instant claims include the ratio between the length and the width of the crystals in the claimed compound. The Caron et al. reference differs from the instant claims because Caron et al. do not include the ratio between the length and the width of the crystals.
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> However, specifying the ratio between the length and width of crystals is an obvious variation absent a showing of unexpected results (see In re Grose and Flanigen, 201 USPQ 57, CCPA 1979). Further, the instant crystalline compounds have the same utility as the crystalline compounds of Caron et al. (see In re Weijard, 1946 C.D. 175, 69 USPQ 86). One of ordinary skill in the art would be motivated [sic, to] use the teachings of

> Caron et al. in the expectation that varying lengths and widths of crystals would improve the usefulness of the compound in pharmaceuticals.
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> Applicant argues that the instant compound is highly electrostatic in nature, difficult to filter and dry and displays poor flowability. However, applicant has not shown unexpected results by way of experimental evidence from a side by side comparison of the prior art compound versus the instantly claimed compound.

This rejection is traversed and reconsideration and withdrawal thereof are requested for the reasons given hereinbelow.

Caron et al., disclose a process for preparing two different crystalline forms, Forms A and B, of 2-n-butyl-4-spirocyclopentane-1-[(2'-(tetrazol-5-yl)biphenyl-4-yl)methyl]-2-imidazolin-5-one. Form A is described as being in the form of stable, non-hygroscopic needles of high electrostatic nature in which the hydrogen atom of the tetrazole ring is in the 1-position. Form B is described as being constituted by triclinic crystals of the tautomer having the hydrogen atom of the tetrazole ring in the 2-position (see column 3, lines 3-15 of Caron et al.). The instantly claimed invention, on the other hand, is directed to a novel crystalline habit of Form A of irbesartan wherein the ratio between the length and the width of the crystals is between 1:1 and 10:1 and to processes for preparing the same.

Initially, applicants would point out that on page 2, lines 15-23 of the instant application is stated that the acicular crystal habit of Form A which is described in Caron et al., is difficult to filter and dry, displays poor flowability and has a high electrostatic nature. What applicants have unexpectedly discovered is that the instantly claimed novel crystal habit of irbesartan has less of a tendency to break or to aggregate when wet, it can be filtered and dried faster and it is easier to handle when it is dry than the acicular crystal habit of Form A described in Caron et al. Of particular note in this regard is the unexpected discovery that (a) the chargeability of the instantly claimed crystal habit of irbesartan was only between 0-10 nanocoulomb/g, compared to the acicular crystal habit of Form A of Caron et al., which was –30 to –40 nanocoulomb/g, which indicates that the instantly claimed crystal habit of

irbesartan has a substantially reduced tendency to store electrostatic charges and can be handled more easily and safely, and (b) the packing density of the instantly claimed crystal habit of irbesartan was approximately 50% greater (0.5 kg/m^3 versus 0.35 kg/m^3) than that for Form A of Caron et al., and the flowability index was 3 times greater (30 versus 10) than that for Form A of Caron et al., which means that the chemical processability of the instantly claimed crystal habit of irbesartan will be substantially improved. Accordingly, the instantly claimed novel crystal habit of irbesartan surprisingly solved each of the problems associated with Form A of Caron et al., i.e., highly electrostatic in nature, difficult to filter and dry and displays poor flowability.

Applicants would also point out that the Examiner's statement that the instant compound is highly electostatic in nature, difficult to filter and dry and displays poor flowability is simply incorrect as the specification clearly sets forth that it is the compound of Caron et al., not the instantly claimed compound, that displays these properties. As noted above, it is the instantly claimed novel crystal habit of irbesartan that has surprisingly solved each of the problems associated with Form A of Caron et al.

Turning now to the Examiner's statement that "applicant has not shown unexpected results by way of experimental evidence from a side by side comparison of the prior art compound versus the instantly claimed compound", applicants would point out that this statement is simple incorrect. As was pointed out hereinabove (as well as in applicants prior Response and Amendment which was mailed on February 5, 2003), on page 2, lines 15-23 of the instant specification, there is provided the comparative tests results for the compound of Caron et al. versus the instantly claimed compound which results clearly and unequivocally demonstrate that unexpected results were indeed obtained for the instantly claimed compound.

Surely it can not be said that there is any disclosure contained in Caron et al., which could possibly teach or suggest to one skilled in the art that irbesartan could even exist in another crystal habit other than the two disclosed in Caron et al., let

alone that such a novel crystal habit, if discovered, would surprisingly solve all of the problems associated with the prior art crystal habit of Form A. Accordingly, contrary to the Examiner's assertion, the disclosure contained in Caron et al., would have provided absolutely no motivation for one of ordinary skill in the art to vary the length and width of the prior art crystals of irbesartan let alone to develop a crystal habit of irbesartan with the specific ratios specified in the instant claims. Thus, it is submitted that the Caron et al., reference is inadequate to render applicants' claimed invention obvious. Neither Caron et al, nor any other references of which applicants are aware has any teaching or suggestion which would have led a person of ordinary skill in the art to applicants' claimed invention. The claimed invention would, therefore, not have been obvious to such a person at the time the invention was made and, hence, the rejection of claims 1-3, 28, and 41-42 based on said reference is believed to be unwarranted and should be withdrawn.

In view of the foregoing remarks, reconsideration and withdrawal of the rejection of claims 1-3, 28, and 41-42 is requested and allowance of claims 1-3, 28-30 and 41-42 is respectfully requested.

Respectfully submitted,

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